REMARKS

Claims 1-41 are currently pending. Claims 1, 2, 4, 6, 7, 19-23 and 26 are currently under examination and are currently rejected. Claims 3, 5, 8-18, 24, 25 and 27-41 are currently withdrawn from consideration. Claim 1 is currently amended.

Support for the amendment to Claim 1 is found throughout the specification, and in particular, on page 4 at lines 14-29, and as illustrated by non-limiting exemplary embodiments presented in Figures 1A to 1J, 3A to 3J, 23, 43, 44, 52 and 53. The amendment to Claim 1 does not introduce new matter.

Claim Rejections

Rejections under 35 U.S.C. §102

Claims 1, 2, 4, 6, 7, 19, 20, 21, 22, and 26 stand rejected under 35 U.S.C. §102(b), as allegedly anticipated by Müller *et al.* in view of WO 97/01580. Applicants respectfully traverse this rejection for the reasons presented below.

To anticipate a claim, the reference must teach every element of the claim. "'A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.'" MPEP § 2131, quoting *Verdegaal Bros. v. Union Oil Co. of California,* 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Here, Claim 1 recites a multifunctional compound having two polypeptide chains, wherein one polypeptide chain includes the constant CH1-domain of an immunoglobulin heavy chain and the other polypeptide chain includes the constant CL-domain of an immunoglobulin light chain, and the polypeptide chains further include, fused to the constant domains, at least two polypeptide functional domains having different receptor or ligand functions, wherein at least one of the functional domains includes a non-immunoglobulin portion having receptor or ligand function, and further wherein at least two of the different functional domains lack an intrinsic affinity for one another and the polypeptide chains are linked via the immunoglobulin constant domains.

In contrast, Müller *et al.* discloses a bispecific antibody (heterodimer) that includes two monomers, one monomer including the CH1-domain linked to VH and VL of an anti-EGF-R scFv fragment, and the other monomer including the CL1-domain linked to VH and VL of an anti-CD2 scFv fragment, *i.e.*, the functional domains fused to the constant domains are immunoglobulin functional domains. Müller *et al.* does not disclose the multifunctional compound of Claim 1, wherein at least one of the functional domains fused to the constant domains includes a non-immunoglobulin portion having receptor or ligand function.

Because Müller *et al.* does not disclose each and every element as set forth in Claim 1, the rejection of Claim 1, and dependent Claims 2, 4, 6, 7, 19, 20, 21, 22, and 26, under 35 U.S.C. §102(b) is improper and should be withdrawn.

Rejections under 35 U.S.C. §103

Claims 1, 2, 4, 6, 7, 19, 20, 21, 22, and 26 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Müller *et al.* in view of Plückthun and Pack. According to the Office Action, Müller *et al.* allegedly discloses a multifunctional compound with all the structural limitations of the rejected claims, but it is admitted that Müller *et al.* does not specifically teach the upper hinge region of human IgG3. Plückthun and Pack allegedly teach the use of hinge regions, in particular the upper hinge from human IgG3. According to the Office Action, it would allegedly have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the linkers of Müller *et al.*, with the upper hinge region of human IgG3 taught by Plückthun and Pack, to make a multifunctional compound. Applicants respectfully traverse for the reasons presented below.

Criteria for establishing a prima facie case of obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference, or references when combined, must teach or suggest all the claim limitations. *See*, MPEP §§ 2142, 2143

The combined references do not provide a suggestion or motivation to make the claimed invention

According to the MPEP, the prior art must suggest the desirability of the claimed invention. MPEP §2143.01 Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988); *In re Jones* 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *See generally*, MPEP §2143. As discussed in detail above, Müller *et al.* discloses expressing a bispecific antibody of two scFv fragments in *E. coli*. Applicants find no teaching or suggestion in Müller *et al.* to produce the multifunctional compound of Claim 1, wherein at least one of the functional domains fused to the constant domains includes a non-

immunoglobulin portion having receptor or ligand function. Applicants find no teaching or suggestion in the secondary reference, Plückthun and Pack, which discloses multivalent and bispecific antibody fragments, to modify the bispecific antibodies of Müller *et al.* to produce the multifunctional compound of Claim 1. Therefore, the cited references do not provide a suggestion or motivation to make the claimed invention.

No reasonable expectation of success

The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. MPEP §2143.02, citing *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) Here there is no expectation that modifying or combining Müller *et al.*, which discloses expressing a bispecific antibody of two scFv fragments in *E. coli*, in view of Plückthun and Pack, which discloses multivalent and bispecific antibody fragments, would be successful to produce the multifunctional compound of Claim 1. Therefore, there is no reasonable expectation of success.

The combination of references does not teach or suggest all claim limitations

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Here, neither Müller *et al.*, which discloses expressing a bispecific antibody of two scFv fragments in *E. coli*, nor Plückthun and Pack, which discloses multivalent and bispecific antibody fragments, disclose a multifunctional compound wherein at least one of the functional domains fused to the constant domains includes a non-immunoglobulin portion having receptor or ligand function. Therefore, the cited references do not teach or suggest all the claim limitations of the claimed invention.

Summary

No *prima facie* case of obviousness has been established and therefore, rejection of Claims 1, 2, 4, 6, 7, 19, 20, 21, 22, 23, and 26 under 35 U.S.C. §103(a) is improper and should be withdrawn.

CONCLUSION

Claims 1-41 are currently pending. Claims 1, 2, 4, 6, 7, 19-23 and 26 are currently under examination. Claims 3, 5, 8-18, 24, 25 and 27-41 are currently withdrawn from consideration. Claim 1 is currently amended. Applicants maintain that the amended claims clearly and patentably define the invention, and respectfully request allowance of the claims now pending.

Applicant believes no fees are due. If any fees are due, please charge any fees associated with the submission of this paper to Deposit Account Number 03-3975. The Commissioner for Patents is also authorized to credit any over payments to the above-referenced Deposit Account.

Respectfully submitted,
PILLSBURY WINTHROP SHAW PITTMAN LLP

DONNA O. PERDUE
Reg. No. 51166
Tel. No. 858.509.4093
Fax No. 858.509.4010

Date: May 19, 2006
11682 El Camino Real,Suite 200
San Diego, CA 92130-2092
(619) 234-5000

CERTIFICATION UNDER 37 C.F.R. §§ 1.8 and/or 1.10*

I hereby certify that, on the date shown below, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: May 19, 2006

Signature

SACHIKO Y. SNEDDEN
(type or print name of person certifying)

** Only the date of filing (§ 1.6) will be the date used in a patent term adjustment calculation, although the date on any certificate of mailing or transmission under § 1.8 continues to be taken into account in determining timeliness. See § 1.703(f). Consider "Express Mail Post Office to Addressee" (§ 1.10) or facsimile transmission (§ 1.6(d)) for the reply to be accorded the earliest possible filing date for patent term adjustment calculations.*